



A PROSPECTIVE ANALYSIS OF RISK FACTORS, PRESENTATION AND OUTCOME OF LEAKAGE AFTER GASTROINTESTINAL ANASTOMOSES

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ABSTRACT **Background:** Despite advancements in modern surgery and postoperative care, disruption of gastrointestinal anastomosis remains the most dreaded complication, even in experienced surgical hands. The cause of leakage is multifactorial consisting of a complete spectrum of pre, intra and postoperative factors. Search for an ideal gastrointestinal anastomosis still remains an unquenched thirst.

Study Design: Prospective, hospital based, time bound observational study.

Methods: After ethical clearance, 288 consenting adult patients who underwent gastrointestinal anastomosis were observed for risk factors, presentation and outcome of leakage and evaluated using appropriate statistical tools.

Results: An overall gastrointestinal anastomotic leak rate of 15.28% with peak incidence at 41-50 years (19.51%) was seen. Peritonitis ($p=0.0009$, $OR=2.9611$), COPD ($p=0.0181$, $OR=2.7306$), low serum albumin concentration ($p=0.0028$, $OR=3.1442$), ASA status of $\geq III$ ($p=0.0001$, $OR=4.0281$) and a perioperative blood transfusion requirement of ≥ 2 units ($p=0.0028$, $OR=3.1442$) were the most significant risk factors associated with leakage. Obstruction ($p=0.0160$, $OR=2.2310$), malignancy ($p=0.0149$, $OR=2.6961$), steroid therapy ($p=0.0176$, $OR=2.2741$), chemoradiation ($p=0.0400$, $OR=2.4889$), diabetes ($p=0.0427$, $OR=2.2689$), undernutrition ($p=0.0308$, $OR=2.1099$), anaemia ($p=0.0325$, $OR=2.0183$) and sepsis ($p=0.0187$, $OR=2.2702$) also showed clear risk augmentation. Risk of leakage was increased with a surgical duration of >4 hours ($p=0.0078$, $OR=2.5610$), when anastomosis was done as an emergency procedure ($p=0.0427$, $OR=2.6571$) or by a surgeon with expertise of ≤ 5 years ($p=0.0338$, $OR=2.7733$). Neither the level, type, technique of anastomosis; nor the usage of surgical staplers had an impact on leakage. Preoperative bowel preparation and creation of a proximal stoma also had minimal effect on leakage rates; though, the infectious complications that follow were greatly reduced. The most common presentation of anastomotic leak was a suspicious drain output with a mean time of $7.59 \pm 2(2.48)$ postoperative days; resulting in a prolongation of hospitalization by more than ten days ($p<0.0001$), along with an increased mortality rate ($p<0.0001$).

Conclusions: Accurately predicting anastomotic leakage still requires more evidence-based information. Even with good risk stratification, many causative factors may not be amenable to immediate correction in the pre-operative period. In such cases, the patient must be considered as a candidate for an enterostomy to help tide the crisis over.

KEYWORDS : Gastrointestinal anastomosis; anastomotic leak.

INTRODUCTION

Gastrointestinal anastomosis is one of the most commonly performed surgical procedure whether in the emergency or in the elective setting. Despite advancements in modern surgery and postoperative care, disruption and leakage of gastrointestinal anastomosis remains the most dreaded complication, even in the most experienced surgical hands. It is often associated with increased morbidity and mortality, apart from an increased healthcare burden, prolonged hospital stay and unnecessary medical expenses¹.

The cause of leakage is, generally, multifactorial; consisting of a complete spectrum of pre, intra and postoperative factors. Previous studies have shown older patients, male gender, obesity and smoking and alcohol abuse as some of the preoperative risk factors that might contribute to anastomotic leakage². General condition of the patient (anaemia, hypoproteinemia, malnourishment & nutritional deficiencies) before the surgery and coexisting diseases decrease the ability of the patient to bear the surgical insult and affect the process of wound healing adversely².

Intraoperatively, faulty suturing technique, ischaemia at the suture line, excessive tension across the anastomosis and mesentery, presence of local sepsis as in case of emergency procedures and a longer duration of surgery may contribute to leakage^{3,4,5}. Parenteral nutrition, antibiotics, blood transfusion and general postoperative patient care also have a bearing on the same. Patients receiving high dose steroids or chemoradiotherapy in the perioperative period may be more prone to leaks⁶. Oesophageal anastomotic leakage is the most important early complication, with incidences of even up to 53% being reported; while, leakage rates following colorectal anastomosis vary from 4 to 26%^{1,7}.

Resection and anastomosis of bowel is always accompanied by some risks and should be avoided wherever possible. The absolute

indication arises when the blood supply of a segment has been so seriously interfered that gangrene, if not previously present, is considered to be inevitable. It may also be required in cases of extensive injuries to gut and its mesentery like penetrating and blunt abdominal trauma. The risk greatly increases in the presence of distal intestinal obstruction, which usually coexists with strangulation. However, when the viability of bowel is suspicious, such risks must be accepted.

The most important critical factor affecting the initial integrity of gastrointestinal anastomoses is the mechanical approximation of the edges to form a completely water tight seal². The serosal layer possesses a high tensile strength to support suturing and therefore, achieving inversion of the bowel edges is important for good apposition. Tension across the anastomosis exerts a mechanical force that can lead to ischaemia causing disruption of integrity⁴.

Surgeons are familiar with the potentially devastating consequences of leakage with patients developing abdominal pain, tachycardia, high grade fever and a rigid and tense abdomen, often accompanied by hemodynamic instability. In these cases, re-exploration with peritoneal washout and fecal diversion is generally required⁸. The mortality rate for an anastomotic leak in literature, typically, is in the range of 6 to 39% along with a 10 to 100% rise of permanent stoma⁹.

However, few patients who develop an insidious presentation of low grade fever, poor appetite, prolonged postoperative ileus or failure to thrive; are often discharged from the hospital without the correct diagnosis in view of early rehabilitation after surgery and cost containment as their non specific symptoms may not justify continued hospitalization. Radiological imaging is usually required to diagnose their grave condition and even then, the diagnosis may remain uncertain⁸. Search for an ideal gastrointestinal anastomosis, therefore, still remains an unquenched thirst.

So, in this study, we aim to identify the risk factors contributing to leakage after gastrointestinal anastomoses along with its presentation and outcome in terms of morbidity and mortality.

MATERIAL AND METHODS

After ethical clearance, the study was conducted on 288 consenting adult patients who underwent gastrointestinal anastomosis at the Department of General Surgery, G.S.V.M. Medical College & L.L.R. Hospital, Kanpur, from January 2019 to October 2020.

Type of study:

Prospective, hospital based, time bound observational study.

Inclusion Criteria:

Consenting adult (age ≥18 years) patients who underwent gastrointestinal anastomosis involving any part of the gut at our tertiary care centre, either in the elective or emergency setting.

Exclusion Criteria:

- Age <18 years
- Pregnant and lactating women
- Patients who underwent primary closure of a small perforation
- Patients who were transferred from outlying hospitals with anastomotic leak, abscess or fistula were excluded unless they redeveloped the complication of leakage after surgery at our institution.

Period of evaluation and end point:

- All subjects were observed during their period of hospitalization and evaluated for anastomotic leakage until their successful recovery/ mortality.

Plan of analysis of data:

- The data collected in pre-designed case report forms was analyzed using statistical tools. A p value of <0.05 corresponding to 95% confidence limits was considered statistically significant.

RESULTS

In a total of 288 subjects evaluated during their period of hospitalization, an overall anastomotic leakage rate of 15.28% (n=44) was observed. The age distribution ranged from 18 to 78 years with a mean age of 38.29 ± 2(14.09) years. The most common age group undergoing gastrointestinal anastomosis was 31-40 years (36.11%). Leakage was most commonly observed among 41-50 years age group (19.51%).

RISK FACTOR	VARIABLES	LEAKAGE PRESENT		LEAKAGE ABSENT		P Value	Odds Ratio
		NO.	%	NO.	%		
Age	≤20 yrs	02	12.50	14	87.50	0.9591	0.782
	21-30 yrs	08	11.76	60	88.24		
	31-40 yrs	16	15.38	88	84.62		
	41-50 yrs	08	19.51	33	80.49		
	51-60 yrs	05	16.67	25	83.33		
	61-70 yrs	04	18.18	18	81.82		
	≥71 yrs	01	14.29	06	85.71		0.923
Sex	Males	32	16.93	157	83.07	0.2820	1.478
	Females	12	12.12	87	87.88		
H/o Hypertension	Present	09	17.65	42	82.35	0.6048	1.237
	Absent	35	14.77	202	85.23		
H/o Cardiac Disease	Present	08	25.00	24	75.00	0.1055	2.037
	Absent	36	14.06	220	85.94		
H/o Past Abdominal Surgery	Present	10	16.95	49	83.05	0.6895	1.171
	Absent	34	14.85	195	85.15		
H/o Smoking	Present	15	21.13	56	78.87	0.1152	1.737
	Absent	29	13.36	188	86.64		
H/o Alcoholism	Present	18	19.15	76	80.85	0.2045	1.530
	Absent	26	13.40	168	86.60		
Blood Urea Nitrogen	>25 mg/dL	18	20.93	68	79.07	0.0824	1.792
	≤25 mg/dL	26	12.87	176	87.13		

Serum Creatinine	>1.5 mg/dL	17	21.79	61	78.21	0.0614	1.889
	≤1.5 mg/dL	27	12.86	183	87.14		
Serum Bilirubin	>1.5 mg/dL	14	22.22	49	77.78	0.0836	1.857
	≤1.5 mg/dL	30	13.33	195	86.67		
Bowel Preparation	Not Done	39	17.33	186	82.67	0.0674	2.432
	Done	05	07.94	58	92.06		
Level of Anastomosis	Stomach- S.I.	02	12.50	14	87.50	0.7779	0.782
	S.I.- S.I.	27	14.52	159	85.48		
	S.I.- L.I.	11	15.94	58	84.06		
	L.I.- L.I.	04	23.53	13	76.47		
Type Of Anastomosis	End to End	38	16.17	197	83.83	0.6329	1.511
	End to Side	04	10.26	35	89.74		
	Side to Side	02	14.29	12	85.71		
Technique Of Anastomosis	Single Transmural	06	12.50	42	87.50	0.5064	0.759
	Single Submucosal	04	10.00	36	90.00		
	Double Layer	30	17.96	137	82.04		
	Stapled	04	12.12	29	87.88		
Material Used For Anastomosis	Silk	16	18.39	71	81.61	0.6994	1.392
	Vicryl	05	11.36	39	88.64		
	PDS	19	15.32	105	84.68		
	Metallic Staples	04	12.12	29	87.88		
Proximal Stoma Formation	Present	09	10.59	76	89.41	0.1530	0.568
	Absent	35	17.24	168	82.76		

RISK FACTORS	VARIABLES	LEAKAGE PRESENT		LEAKAGE ABSENT		P VALUE	ODDS RATIO
		NO.	%	NO.	%		
		P/w Peritonitis	Present	26	24.53		
	Absent	18	09.89	164	90.11		
P/w Obstruction	Present	19	23.46	62	76.54	0.0160	2.231
	Absent	25	12.08	182	87.92		
H/o DM	Present	10	26.32	28	73.68	0.0427	2.269
	Absent	34	13.60	216	86.40		
H/o COPD	Present	09	30.00	21	70.00	0.0181	2.731
	Absent	35	13.57	223	86.43		
H/o Chemoradiotherapy	Received	08	28.57	20	71.43	0.0400	2.489
	Not Received	36	13.85	224	86.15		
H/o Steroid Therapy	Present	16	24.62	49	75.38	0.0176	2.274
	Absent	28	12.56	195	87.44		
Under Nutrition	<18.5 kg/m ²	16	23.53	52	76.47	0.0308	2.110
	≥18.5 kg/m ²	28	12.73	192	87.27		
Hb	<10 gm/dL	21	21.65	76	78.35	0.0325	2.018
	≥10 gm/dL	23	12.04	168	87.96		
Sepsis	Present	31	19.87	125	80.13	0.0187	2.270
	Absent	13	09.85	119	90.15		
Serum Albumin	<3.0 gm/dL	12	31.58	26	68.42	0.0028	3.144
	≥3.0 gm/dL	32	12.80	218	87.20		
ASA Grade	III-V	27	28.13	69	71.87	0.0001	4.028
	I-II	17	08.85	175	91.15		
Surgeon Expertise	≤5 Years	39	17.81	180	82.19	0.0338	2.773
	>5 Years	05	07.25	64	92.75		
Type Of Surgery	Emergency	39	17.65	182	82.35	0.0427	2.657
	Elective	05	07.46	62	92.54		
Duration Of Surgery	>4 hrs	15	26.79	41	73.21	0.0078	2.561
	≤4 hrs	29	12.50	203	87.50		
BT	≥2 units	12	31.58	26	68.42	0.0028	3.144
	<2 units	32	12.80	218	87.20		
Biopsy	Malignant	10	29.41	24	70.59	0.0149	2.696
	Benign	34	13.39	220	86.61		

PRESENTATION	NO.	%
Enterocutaneous Fistula formation	07	15.91
Evidence of sepsis	13	29.55
Suspicious drain output	20	45.45
Subclinical (Radiological evidence)	04	09.09
OVERALL	44	100.00

POST-OP DAY (P.O.D.)	NO.	%
≤3	02	04.55
4 to 7	18	40.91
8 to 11	23	52.27
≥12	01	02.27
OVERALL	44	100.00

X=7.59 days; σ=2.48 days

LEAKAGE	EXPIRY		RECOVERY		TOTAL	
	NO.	%	NO.	%	NO.	%
Present	24	54.55	20	45.45	44	15.28
Absent	21	08.61	223	91.39	244	84.72
OVERALL	45	15.63	243	84.38	288	100.00

$\chi^2=59.466$; $p<0.0001$, highly significant

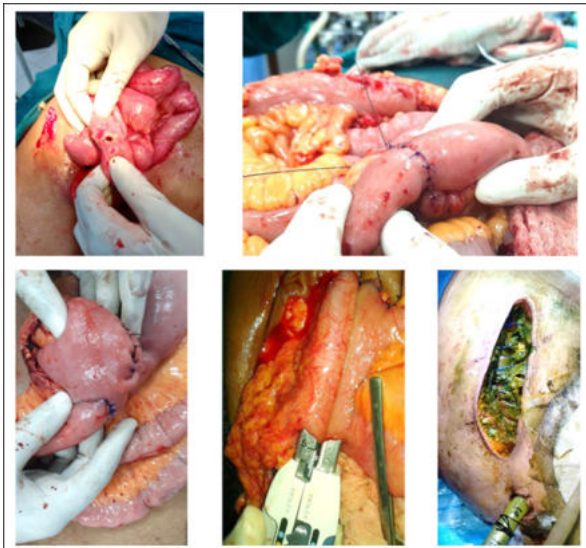


Figure 1: (From top left corner) Small bowel perforation; double layered end-to-end bowel anastomosis, end-to-side anastomosis, side to side stapler anastomosis, enterocutaneous fistula.

DISCUSSION

An overall leakage of 15.28%, favorably comparable to 16% reported by Jina A., et al (2019), was observed¹⁰. Such high leakage rate may be attributed to the delayed presentation of patients to this teaching hospital usually in a debilitated condition as an emergency.

In our study, a mean age of $38.29 \pm 2(14.09)$ years was seen, probably due to the higher prevalence of bowel perforations and traumatic injuries to abdomen affecting individuals in the prime of their lives. Higher mean ages reported in other studies could be a reflection of the higher incidence of colorectal malignancies in old age. Increasing age as a risk factor for leakage was not significant ($p=0.9591$). The male to female ratio of subjects was 1.91:1. Leakage in males (16.93%) was more common than in females (12.12%) but was not significant ($p=0.2820$). Mäkelä, et al (2003) had also shown that age and sex did not affect the incidence of leakage¹¹.

Established peritoneal contamination is a well identified independent risk factor for increased morbidity after bowel anastomosis³. A leak rate of 24.53% was observed in subjects with peritonitis as compared to 9.89% leaks in subjects without peritonitis. This highly significant difference ($p=0.0009$; OR=2.9611) can be attributed to increased lysis of collagen due to enhanced collagenase activity in infected anastomoses. A significant ($p=0.0160$; OR=2.2310) increase in leak rates from 12.08% to 23.46% was also observed in the presence of obstruction which can be due to ischemia caused by raised intraluminal

pressure due to distal obstruction.

Diabetes is categorized among negative factors mitigating intestinal anastomosis². However, its direct effect on the healing process is difficult to separate from an indirect impairment caused via increased infection. A significant difference ($p=0.0427$; OR=2.2689) was seen with 26.32% leaks in diabetic subjects as compared to 13.60% leaks in non-diabetics. Leakage also rose significantly ($p=0.0181$; OR=2.7306) from 13.57% to 30.00% in subjects with COPD; which is in agreement with Alves A., et al (2002) who found respiratory comorbidity as an independent risk factor for leaks³.

Leakage in subjects with cardiac disease (25.00%) was more common than those without any cardiac disease (14.06%) but this difference was found to be not significant ($p=0.1055$). Similarly, leakage in hypertensives (17.65%) was more common than in normotensives (14.77%) but was also not significant ($p=0.6048$). Hamed Ahmed Abd El Hameed El-Badawy, et al (2014) and Ramula M., et al (2016) also reported parallel findings respectively^{12,13}.

Subjects with history of prior abdominal surgery had a leakage of 16.95% as compared to 14.85% leaks in opposite group. This difference, however, was not significant ($p=0.6895$). It may be due to most patients with prior surgery being operated electively for stoma closures as against other emergency cases.

David W. Dietz, et al (2003) stated increased leakage in patients on >40mg per day of prednisolone and in those who received neoadjuvant chemoradiation⁶. Likewise, we observed a significant increase in leakage from 13.85% to 28.57% in subjects who had received chemoradiation ($p=0.0400$; OR=2.4889); and from 12.56% to 24.62% in subjects with history of steroid therapy ($p=0.0176$; OR=2.2741).

Frances Goulder, et al (2001) had categorized smoking and alcohol among negative factors mitigating intestinal anastomosis². In this study, although leakage rose from 13.36% to 21.13% in smokers ($p=0.1152$) and from 13.40% to 19.15% in subjects with history of alcoholism ($p=0.2045$); but, this difference was found to be not significant.

Malnourished patients and those with hypoalbuminemia may be at increased risk of deranged anastomotic healing due to attenuated immunocompetence or lack of essential amino acids for collagen synthesis¹⁴. Consistently, we observed a significant increase in leakage from 12.73% to 23.53% in subjects with BMI <18.5kg/m² ($p=0.0308$; OR=2.1099); and from 12.80% to 31.58% in cases with serum albumin <3.0gm/dL ($p=0.0028$; OR=3.1442). Also, subjects with hemoglobin <10gm/dL had a significant ($p=0.0325$; OR=2.0183) leakage of 21.65% as compared to 12.04% leaks in subjects with hemoglobin ≥10gm/dL, similar to findings of Faisal Bilal, et al (2006)¹⁵.

In this study, subjects with evidence of sepsis had a significant ($p=0.0187$; OR=2.2702) rise in leakage from 9.85% to 19.87%. Golub, et al (1997) and Alves A., et al (2002) also found significant parallel results^{16,3}.

Although, leakage rose from 12.87% to 20.93% in subjects with B.U.N. >25mg/dL ($p=0.0824$) and from 12.86% to 21.79% in subjects with serum creatinine >1.5mg/dL ($p=0.0614$); but, this difference was found to be not significant. Cases with serum bilirubin >1.5mg/dL also reported leakage rise from 13.33% to 22.22% which not significant ($p=0.0836$).

ASA grading of III or more is an independent risk factor for the development of anastomotic leakage¹⁷. In our study, leakage rate rose from 8.85% in ASA grades I-II to 28.13% in ASA grades III-V which was highly significant ($p=0.0001$; OR=4.0281).

Burke P., et al. (1994) had questioned the use of bowel preparation showing no difference in outcomes after colon surgery between prepared and unprepared patients¹⁸. In our study, leakage in subjects without bowel preparation (17.33%) was more common than leakage in those with bowel preparation (7.94%); but, this difference was not significant ($p=0.0674$). Some controversies have recently developed with a few contrasting studies, but these may be due to other co-existing confounding variables like elective or emergency surgical procedure.

Several studies in the past have shown experience of the surgeon to be

insignificant in determining the leakage rates. In sharp contrast, we found a significant difference ($p=0.0338$; $OR=2.7733$) in leak rates of anastomoses done by surgical residents with ≤ 5 years experience (17.81%) as compared to a consultant surgeon with >5 years experience (7.25%). Ragg A.L., et al (2009) concluded that low surgeon case volume was an independent risk factor for mortality¹⁹. Philips Kirchoff, et al (2011) also concluded that experience of the surgeon was a predictive risk factor for anastomotic complications²⁰.

Leakage in anastomosis done as an emergency procedure (17.65%) was significantly ($p=0.0427$; $OR=2.6571$) more common than in those performed electively (7.46%). Faizal Bilal, et al (2006) had also observed anastomotic dehiscence of 75% in emergency cases versus 25% in elective ones¹⁵.

David W. Dietz, et al (2003) reported lowest leak rates (3%) after small bowel and ileo-colic anastomoses, highest after colo-anal anastomoses (10-20%) and that the risk of leak after low anterior resection of rectum was inversely related to its distance from the anal verge⁶. Likewise, esophageal anastomoses are also known for notorious leakage. However, Golub, et al (1997) reported small bowel leak rate was not significantly different from leak in distal large bowel¹⁶. In our study, maximum cases were of small bowel to small bowel anastomoses (64.58%) followed in decreasing order by small bowel to large bowel (23.96%), large bowel to large bowel (5.90%) and then stomach to small bowel (5.56%); with leakage rates of 14.52%, 15.94%, 23.53% and 12.5% respectively. This difference was not significant ($p=0.7779$). Such results could be because of the extremely low cases of colorectal and esophageal anastomoses in our study that may not truly reflect the leak rates in such procedures. Also, leakage rates in end to end, end to side and side to side anastomoses were 16.17%, 10.26% and 14.29% respectively which was not significant ($p=0.6329$).

Satoru Shikata, et al (2006) concluded that there is no evidence that two layered intestinal anastomosis leads to fewer postoperative leaks than single layered technique²¹. Choy PY, et al (2007) in a Cochrane database review reported that ileocolic stapler anastomosis were associated with fewer leaks than hand sewn anastomosis²². Yet, the best anastomotic technique still remains controversial with literature to support all the techniques but without any single consensus of a particular technique being superior to the rest. In our study, no significant difference ($p=0.5064$) was observed in leakage among single layered transmural hand-sewn (12.50%), single layered submucosal hand-sewn (10.00%), double layered hand-sewn (17.96%) and even a stapled anastomosis (12.12%). However, considering the duration of procedure and the medical expenses, single layered submucosal (Cushing's) anastomosis appears to represent the optimal choice in most situations^{15,21}.

30.21% subjects had GI anastomosis using silk, 15.28% had anastomosis using vicryl suture; in 43.06% subjects PDS was used while 11.46% underwent a stapled procedure. Leakage in respective cases were 18.39%, 11.36%, 15.32% and 12.12% which were found to be not significant ($p=0.6994$). Mohd. U. Nasir Khan, et al (2006) found that the use of sutures or staples to create anastomosis has never been shown to significantly alter the anastomotic leak rate⁴. Still, we cannot differ to agree to the inference of Calin MD, et al (2013) that although, in relation to efficacy, applicability and safety, the use of surgical stapling instruments is comparable to that of conventional suturing methods; but, in certain situations, staplers do offer the facility to accomplish reconstructions that would be manually difficult along with the added advantage of a curtailed operating duration and their popularity in these settings seems justifiable²³.

David W. Deitz, et al (2003) stated that the creation of a diverting stoma proximal to a high risk anastomosis minimizes the severe consequences of a leak, but does not reduce the incidence of leak itself⁶. Lipska M.A., et al (2006) observed that some leaks, undoubtedly, remained unrecognized (subclinical) in the postoperative period due to the creation of a stoma⁵. The re-operation rate after anastomotic leakage in patients with a stoma was lower than that in patients without a stoma, but the leak rate was unaffected. We, too, found no significant difference ($p=0.1530$) between leakage rates in cases with a proximal stoma (10.59%) and in those without any diversion (17.24%).

In the study, significant difference ($p=0.0078$; $OR=2.5610$) was observed in leakage rates of cases with a surgical duration >4 hours (26.79%) as compared to those lasting ≤ 4 hours (12.50%). Multiple studies have identified long operative time as a potential risk factor for

anastomotic leakage^{3,4,5}. Ramula M., et al (2016) proposed that a longer mean operative duration was reflective of the difficulties faced intraoperatively which might later predispose to anastomotic leakage¹³.

Our study showed significantly ($p=0.0028$; $OR=3.1442$) increased leakage in cases with perioperative blood transfusion of ≥ 2 units (31.58%) as against those with transfusion of <2 units (12.80%) which coincides with Mohd. U. Nasir Khan, et al (2006)⁴.

Histopathological examination of resected bowel segment in 11.81% cases was suggestive of malignant disease; out of which 29.41% cases leaked as compared to 13.39% leaks in cases with benign pathology and this difference was significant ($p=0.0149$; $OR=2.6961$). Fazio, et al (2004) observed an even greater odds ratio of 4.5 consistent with our findings²⁴. Kioanka Trencheva, et al (2013) investigated the use of Charlson Comorbidity Index (CCI) for predicting leakage with $CCI>3$ indicating independent risk. Metastatic solid tumors alone have been given a score of 6, the highest in CCI²⁵.

The most common presentation of leakage was a suspicious drain output (45.45%), followed by clinical sepsis (29.55%), enterocutaneous fistula formation (15.91%) and least frequently as subclinical presentation detected radiologically (9.09%). Dendulk, et al. (2009) combined clinical features of leakage into a "Dutch leakage score" indicating cases prone to leak that required intensive clinical observation or radiological evaluation²⁶.

The mean time of evidence of leakage was $7.59 \pm 2(2.48)$ postoperative days. Leak was most commonly evident from P.O.D. 8 to 11 (52.27%). Neil Hyman, et al (2007) also quoted that anastomotic leaks are frequently diagnosed late in the postoperative period and often after initial hospital discharge, highlighting the importance of adequate follow up⁸.

In this study, there was an overall mortality of 15.63%. The difference in mortality among the cases with anastomotic leakage (54.55%) and those without leakage (8.61%) was highly significant ($p<0.0001$). The odds ratio suggested risk of mortality following leakage to be 12.74 times than that of subjects without leaks. Similarly, Brisinda G., et al (2009) had reported anastomotic leakage to be associated with a 6-39% rise in mortality rate and a 10-100% risk of permanent stoma formation⁹.

An estimate of morbidity due to leakage was made by the average duration of hospital stay of the 243 subjects that recovered following anastomoses. Among the 20 (45.45%) leaked cases that recovered, the mean duration of hospitalization was $19.46 \pm 2(1.93)$ days as compared to $9.32 \pm 2(1.24)$ days in 223 (91.39%) recovered cases without any leakage. Standard error of difference between the two means was highly significant ($p<0.0001$) confirming anastomotic leaks as a cause of major morbidity to the patient while being a heavy burden on the healthcare delivery system.

CONCLUSION

- In this study, an overall gastrointestinal anastomotic leak rate of 15.28% with peak incidence at 41-50 years of age was seen.
- Peritonitis, COPD, low serum albumin concentration, ASA grade of more than II and a perioperative blood transfusion requirement of two or more units were the most significant risk factors associated with leakage.
- Obstruction, malignancy, steroid therapy, chemoradiation, diabetes, undernutrition, anaemia and sepsis also showed a clear augmentation of risk.
- Risk of leakage was increased with a surgical duration of more than four hours and when anastomosis was done as an emergency procedure or when performed by residents who were still under the learning curve as compared to the experienced hands of a consultant surgeon.
- Neither the level, type, technique of anastomosis; nor the usage of surgical staplers had an impact on leakage.
- Preoperative bowel preparation and creation of a proximal stoma also had minimal effect on leakage rates; though, the infectious complications that follow were greatly reduced.
- The most common presentation of anastomotic leak was a suspicious drain output with a mean time of $7.59 \pm 2(2.48)$ postoperative days; resulting in a prolongation of hospitalization by more than ten days, along with a mortality rate that was increased by several folds.
- Accurately predicting anastomotic leakage still requires more evidence-based information. Even with good risk stratification,

many of the factors causing disruption may not be amenable to immediate correction in the pre-operative period. In such cases, the patient must be considered as a candidate for an enterostomy to help tide the crisis over.

Limitations

In addition to the variables identified, many other factors may be important determinants of anastomotic dehiscence such as technical construction of the anastomoses, tension on the suture line, adequacy of microcirculation at the anastomotic site, etc. which as yet, remain unquantified.

Conflict Of Interest

The authors disclose no potential conflicts of interest.

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REFERENCES

- Bruce J., Krukowski Z.H., Al-Khairy G., et al. (2001). Systematic review of the definition and measurement of anastomotic leak after gastrointestinal surgery. *British Journal Surg* 2001; 88(9):1157-68.
- Frances Goulder. (2001). Patient and technical factors affecting anastomotic healing. *World Gastrointestinal Surgery*, Sept 27: 208-213; 2001.
- Alves A., Panis Y., Trancart D. (2002). Factors associated with clinically significant anastomotic leakage after large bowel resection: multivariate analysis of 707 patients. *World J Surg.* 26(4):499-502.
- Mohd. U. Nasir Khan. (2006). Anastomotic disruption after large bowel resection. *World J Gastroenterology*; 16: 2497-2504: April 2006.
- Lipska M.A., Bissett I.P., Parry B.R., Merrie A.E. (2006). Anastomotic leakage after lower gastrointestinal anastomosis: men are at a higher risk. *ANZ J Surg.* 2006 Jul; 76(7):579-85. doi: 10.1111/j.1445-2197.2006.03780.x. PMID: 16813622.
- David W. Dietz. (2003). Complication in Colorectal Surgery, *Dis. Colon Rectum.* 38; 749-54: 2003.
- Boccola M.A., Lin J., Rozen W.M., et al (2010). Reducing anastomotic leakage in oncologic colorectal surgery: an evidence-based review. *Anticancer Res.* 30(2):601-7.
- Hyman N., Manchester T.L., Osler T., Burns B., Cataldo P.A. (2007). Anastomotic leaks after intestinal anastomosis: it's later than you think. *Ann Surg.* 2007 Feb; 245(2):254-8. doi: 10.1097/01.sla.0000225083.27182.85. PMID: 17245179; PMCID: PMC1876987.
- Britsinda G., Vanella S., Cadeddu F. (2009). End-to-end versus end-to-side stapled anastomoses after anterior resection for rectal cancer. *J Surg Oncol.* 99(1):75-9.
- Jina, Abhishek; Singh, Umesh Chandra. (2019). Factors influencing intestinal anastomotic leak and their predictive value. *International Surgery Journal, [S.I.]*, v. 6, n. 12, p. 4495-4501, Nov. 2019. ISSN 2349-2902.
- Mäkelä J.T., Kiviniemi H., Laitinen S. (2003). Risk Factors for Anastomotic Leakage After Left-Sided Colorectal Resection With Rectal Anastomosis. *Dis Colon Rectum.* 2003; 46:653-60.
- Hamed Ahmed Abd El Hameed El-Badawy. (2014). Anastomotic leakage after gastrointestinal surgery: risk factors, presentation and outcome. *Egyptian Journal of Hospital Medicine*, Oct 2014, Vol 57, Page 494-512.
- Ramula M., Sankarlingam P., Karthik A. (2016). A study of risk factors influencing anastomotic leak following small bowel obstruction. *Journal of Evolution of Medical and Dental Sciences*; Oct 13, 2016.
- Ketan R. Vagholkar. (2009). Local and systemic factors on intestinal anastomosis. *Bombay Hospital Journal* 54(2): 2009.
- Faizal Bilal. (2006). Anastomotic leakage after small gut surgery. *Professional Medical Journal, Pakistan* 2006.
- Golub R., Golub R.W., Cantu R. Jr., Stein H.D. (1997). A multivariate analysis of factors contributing to leakage of intestinal anastomoses. *J Am Coll Surg.* 1997 Apr; 184(4):364-72. PMID: 9100681.
- Kim S.H., Son S.Y., Park Y.S., Ahn S.H., Park D.J., Kim H.H. (2015). Risk Factors for Anastomotic Leakage: A Retrospective Cohort Study in a Single Gastric Surgical Unit. *J Gastric Cancer.* 2015; 15:167-75.
- Burke P., Mealy K., Gillen P., et al. (1994). Requirement for bowel preparation in colorectal surgery. *Br J Surg.* 81(6):907-10.
- Ragg J.L., Watters D.A., Guest G.D. (2009). Preoperative risk stratification for mortality and major morbidity in major colorectal surgery. *Dis Colon Rectum.* 52: 1296: 2009.
- Philips Kirchoff, Daniel Matz. (2011). Complications in colorectal surgery; Patient Safety in Surgery; 4: 5: 2011.
- Satoru Shikata. (2006). Single versus double layered intestinal anastomosis. *BMC Surgery*; 6: 2: 2006.
- Choy P.Y., Bissett I.P., Docherty J.G., et al (2007). Stapled versus hand sewn methods for ileocolic anastomoses. *Cochrane Database Syst Rev.* (3): CD004320.
- Calin M.D., Bălălu C., Popa F., et al (2013). Colic anastomotic leakage risk factors. *J Med Life*; 6(4):420-3.
- Fazio V. W., Tekkis P. P., Remzi F., Lavery I. C. (2005). Assessment of operative risk in colorectal cancer surgery: the Cleveland Clinic Foundation colorectal cancer model. *Dis Colon Rectum*; 47: 2015: 2005.
- Kioanka Trencheva. (2013). Identifying important predictors for anastomotic leaks after colon and rectal resections. *Annals of Surg*; 257(1): 52-60: Jan 2013.
- Dendulk M., Noter S.L., Hendriks E.R., et al (2009). Improved diagnosis and treatment of anastomotic leakage after colorectal surgery. *Eur J Surg Oncol.* 35(4):420-6.